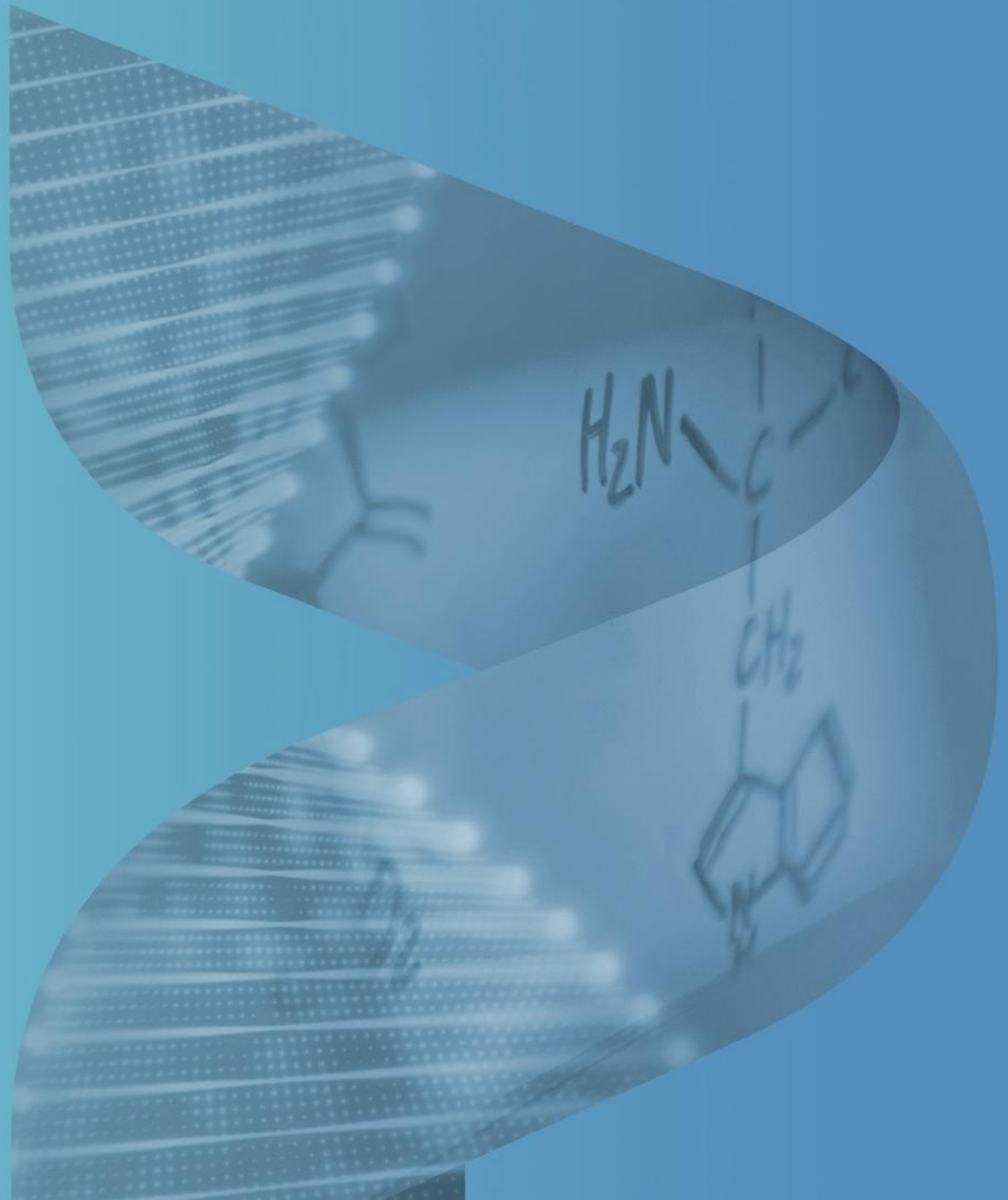
PepGen™

Pioneering RNA-Targeted Therapies for Rare Genetic Diseases

Company Presentation

November 2026



Forward-Looking Statements

This presentation is being made by PepGen Inc. (“PepGen,” “we,” “our,” “us”) and contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will,” and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this presentation that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding the potential of our EDO platform to deliver high levels of oligonucleotide to the nuclei and to deliver to a broad range of tissues, the promising trends and therapeutic potential and safety profile of PGN-EDODM1 based on data from the 5, 10 and 15 mg/kg cohorts of the FREEDOM study and 5 and 10 mg/kg cohorts of the FREEDOM2 trial, PGN-EDODM1's potential to deliver meaningful benefit to the DM1 community, our expectations regarding the timing of data from the 12.5 mg/kg cohort of the FREEDOM2 trial, our expectations on the timing of the 5 mg/kg clinical and 10 mg/kg safety data from the FREEDOM-OLE trial, our plans to initiate an expansion cohort running in parallel to cohort 3, the design, initiation and conduct of clinical trials, including expected timelines for data readouts from our FREEDOM2 and OLE trials, the potential for any functional improvements that may result from splicing correction with PGN-EDODM1, dose-dependent increases in splicing suggesting that PGN-EDODM1 is getting into the muscle and effectively binding to the target, the potential for PGN-EDODM1 to offer a best-in-class treatment option, ongoing and planned regulatory interactions and our financial resources and expected cash runway.

These forward-looking statements in this presentation are based on current expectations, estimates and projections only as of the date of this presentation and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Many actual events and circumstances are beyond PepGen’s control These risks and uncertainties include, but are not limited to: delays or failure to successfully initiate or complete our ongoing and planned development activities for our product candidates, including PGN-EDODM1; our ability to enroll patients in our clinical trials, including FREEDOM2 and OLE trials, that our interpretation of clinical and preclinical study results may be incorrect, or that we may not observe the levels of therapeutic activity in clinical testing that we anticipate based on prior clinical or preclinical results or cross-trial comparisons, including for PGN-EDODM1 and cross-trial comparisons; our product candidates, including PGN-EDODM1, may not be safe and effective or otherwise demonstrate safety and efficacy in our clinical trials; adverse outcomes from our regulatory interactions, including delays in regulatory review, clearance to proceed or approval by regulatory authorities with respect to our programs, including clearance to commence planned clinical studies of our product candidates, including release of the partial clinical hold placed by FDA on the FREEDOM2 study, or other regulatory feedback requiring modifications to our development programs, including with respect to the FREEDOM2 program; changes in regulatory framework that are out of our control; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for the indications we are pursuing; unexpected increases in the expenses associated with our development activities or other events that adversely impact our financial resources and cash runway; and our dependence on third parties for some or all aspects of our product manufacturing, research and preclinical and clinical testing. These forward-looking statements should not be relied upon as representing our assessments as of any date subsequent to the date of this presentation. Additional risks concerning our programs and operations are described in our most recent filings with the U.S. Securities and Exchange Commission. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

This presentation discusses PGN-EDODM1, an investigational therapy, that has not been approved for use in any country, and is not intended to convey conclusions about their efficacy or safety. There is no guarantee that PGN-EDODM1 or any other investigational therapy will successfully complete clinical development or gain regulatory authority approval.

PepGen: Setting a New Standard in RNA-Targeted Therapy for DM1

OUR VISION

Develop therapies that **address the root cause** of serious rare genetic diseases — driving meaningful restoration of function

Backed by a team of **leading drug developers** and founded on **more than a decade** of research and development

EDO TECHNOLOGY

Enhanced Delivery Oligonucleotide

Achieving receptor-independent **broad delivery** with **superior nuclear uptake** of therapeutic oligonucleotides, overcoming key limitations of prior approaches



PGN-EDODM1: *Myotonic Dystrophy Type 1*

- ✓ Highest level of splicing reported in a multiple dose study
- ✓ Improvements in myotonia, mobility, and grip strength
- ✓ Favorable safety profile
- ✓ Orphan Drug & Fast Track Designation (U.S.); Orphan Designation (EU); CMC Development and Readiness Pilot (CDRP) program

WELL POSITIONED FOR VALUE CREATION

Anticipated Upcoming Milestones

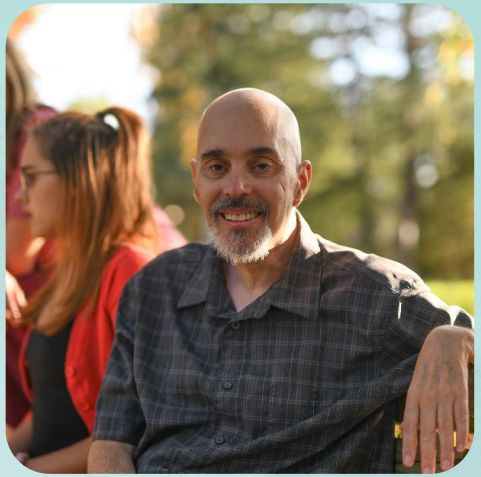
- **January 2027:** Interim FREEDOM-OLE 5 mg/kg clinical and 10 mg/kg safety data expected
- **1H 2027:** FREEDOM2 12.5 mg/kg clinical results expected

Strong cash runway into 2029

At PepGen, we are committed to transforming the lives of people and families living with myotonic dystrophy type 1 (DM1).













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PGN-EDODM1 Seeks to Address the Underlying Cause of DM1

A Rare, Genetic, Multisystemic Disease with No Approved Therapies



Jubal and Family, Living with DM1

Myotonic Dystrophy Type 1 (DM1)

- **Caused by CTG expansion in the *DMPK* gene**, resulting in pathogenic *DMPK* transcripts driving disease pathology
- **More than 110,000 people**[1] affected in the U.S. and EU
- Symptoms can develop from childhood through adulthood with **greater severity in each successive generation**
- **Average life expectancy is 50–60 years** in patients with non-congenital DM1
- **No approved therapies** currently address the underlying cause of the disease

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Sources: Neuroepidemiology (2022) 56 (3): 163–173., Neurology 2021 Feb 16;96(7):e1045-e1053
[1]Some estimates are as much as 5-fold higher prevalence of DM1: Brain (10 Oct 2026), awag250
CTG: cytosine-thymine-guanine; *DMPK*: dystrophia myotonica protein kinase

DM1 is Multisystemic and Addressing the Disease Burden Requires Therapeutic Breadth to Reach, Reset, and Restore Function

THE BURDEN

DM1 impacts multiple systems and daily life

- Skeletal Muscle and Mobility
- Myotonia
- Cognition, sleep and fatigue
- Cardiac and respiratory
- Speech and swallowing
- Gastrointestinal

THE DESIGN REQUIREMENT

01

Reach affected tissues

Enhanced peptides are designed to carry oligonucleotide payloads beyond narrow delivery constraints.

02

Enter the nucleus

The payload must escape the endosome and reach the compartment where disease-driving RNA disrupts cellular function.

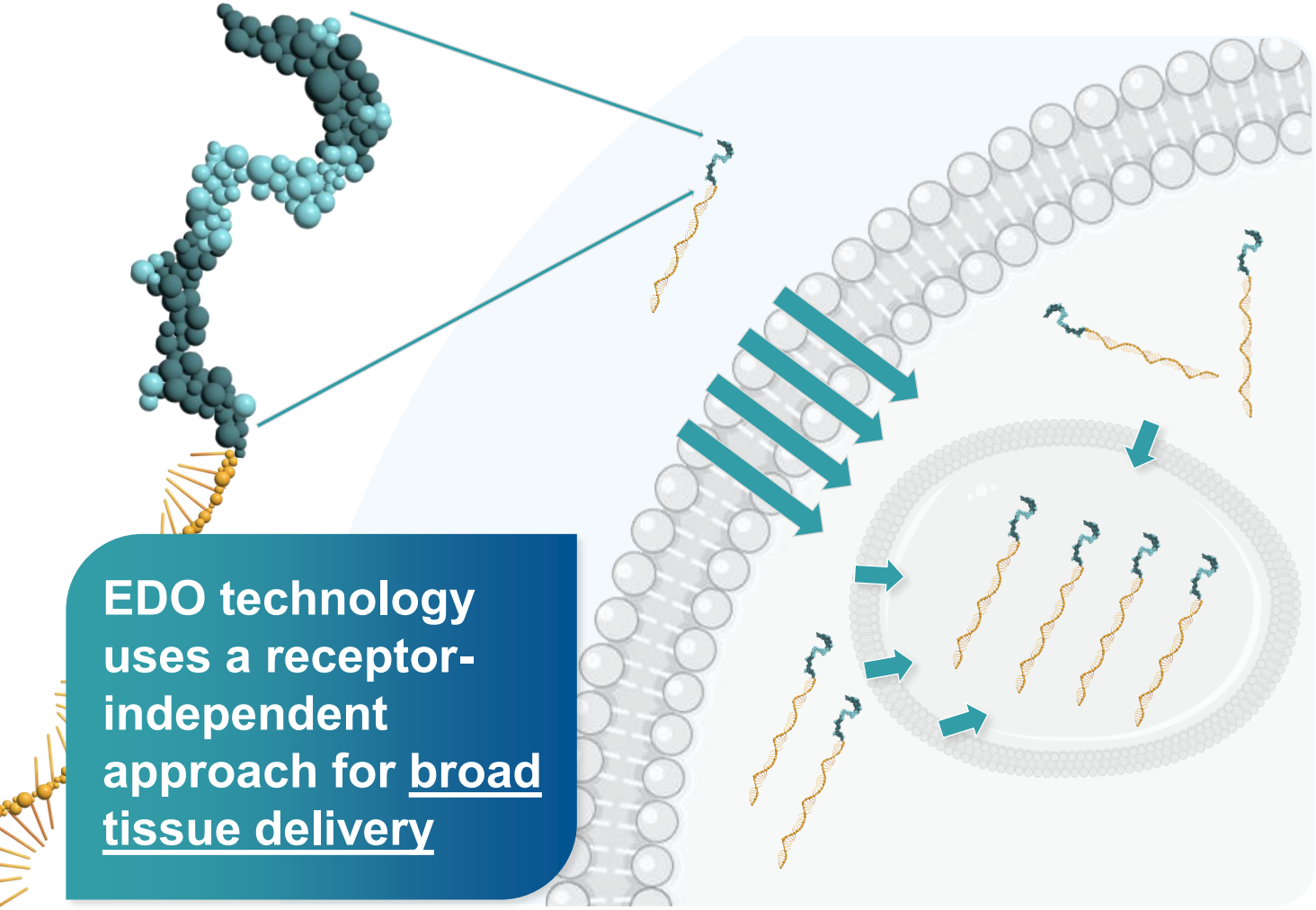
03

Act selectively at the source

Targeted oligonucleotides are designed to bind pathogenic RNA while preserving healthy expression to reset splicing.

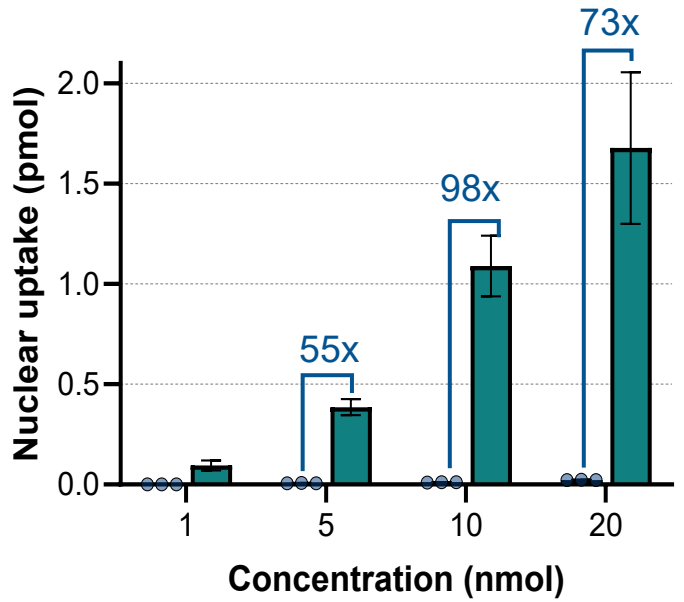
The disease burden defines the therapeutic ambition:
Reach broadly, reset splicing, and restore function

PepGen's EDO Technology is Designed to Reach a Broad Range of Tissues with Optimal Delivery by Endosomal Escape and Superior Nuclear Uptake



EDO technology uses a receptor-independent approach for broad tissue delivery

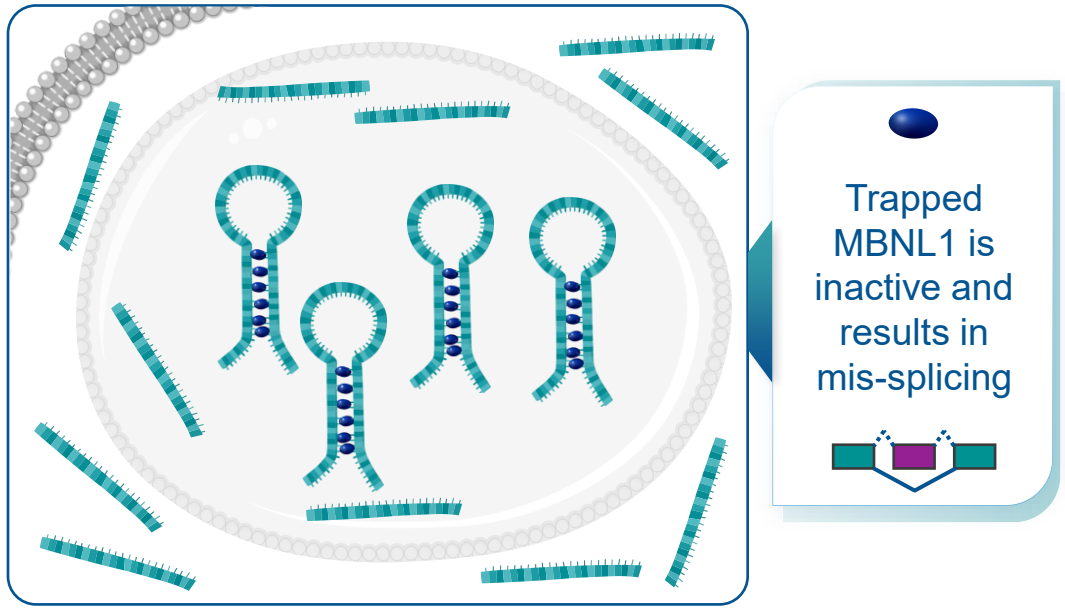
EDO technology results in up to a 98-fold increase in nuclear delivery



Immortalized myoblasts from a healthy individual or a DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes and then treated with fluorescently tagged PGN-PMODM1 (PMO) or PGN-EDODM1 (PPMO) at concentrations detailed above. Cells were visualized by confocal microscopy 24h after treatment. Graphs are presented as mean ± SD.

PGN-EDODM1 Blocking Approach Targets the Pathogenic CUG^{exp} Repeats *DMPK* RNA while Preserving Normal *DMPK*

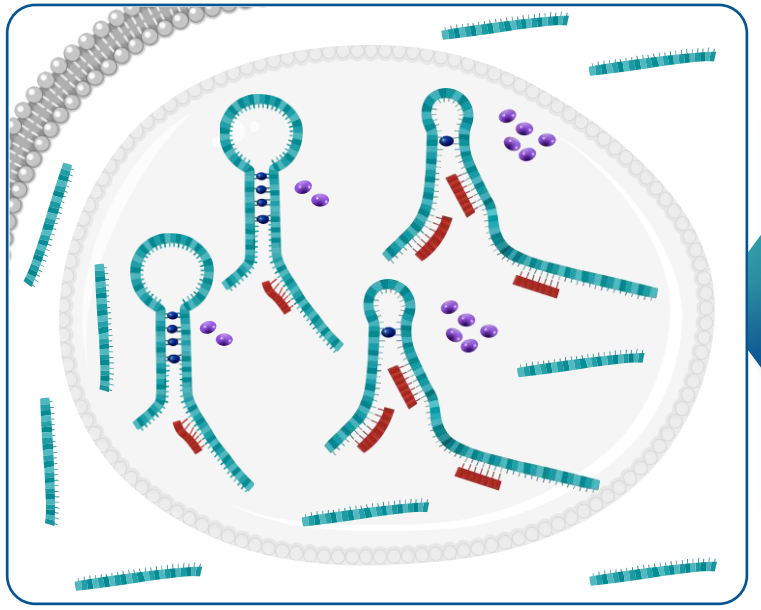
DM1 is caused by pathogenic *DMPK* transcripts



Trapped MBNL1 is inactive and results in mis-splicing

- DM1 is caused by pathogenic *DMPK* transcripts containing CUG^{exp} repeat sequences that form hairpin loops
- These hairpin loops trap MBNL1 proteins that are needed for correct splicing of mRNAs

PGN-EDODM1 binds selectively to the pathogenic *DMPK* transcript



Liberated MBNL1 restores correct splicing

- PGN-EDODM1 binds selectively to the pathogenic *DMPK* transcript, causing steric blocking, but not degrading the RNA
- This reduces the ability of the CUG^{exp} repeats to form hairpin loops and sequester RNA splicing proteins

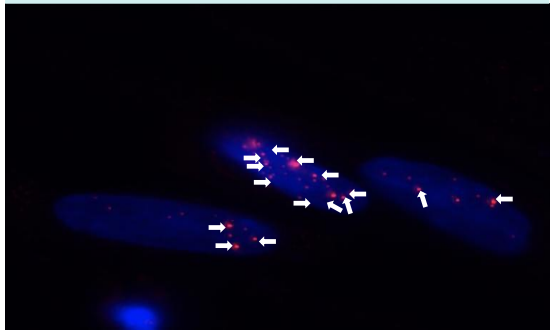
DMPK transcript | Bound MBNL1 (inactive) | PGN-EDODM1 | Free MBNL1 (active)

Wojciechowska, et al., Quantitative Methods to Monitor RNA Biomarkers in Myotonic Dystrophy, *Nature*, April 12, 2018

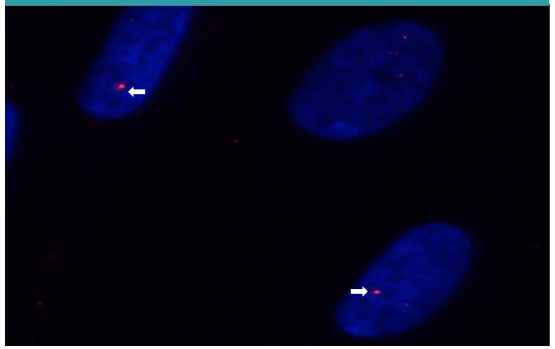
PGN-EDODM1 Reduced Pathogenic Nuclear Foci, Liberated MBNL1 and Corrected Mis-Splicing in Patient Cells with Long CUG Repeats

Foci Reduction

Not Treated



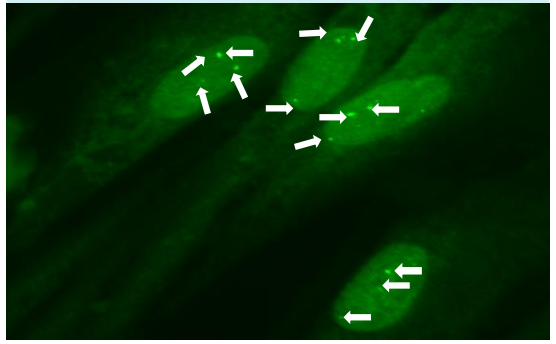
PGN-EDODM1 Treated



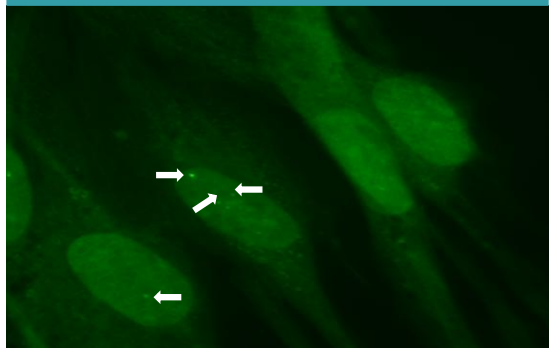
54%
reduction in toxic foci

MBNL1 Liberation

Not Treated



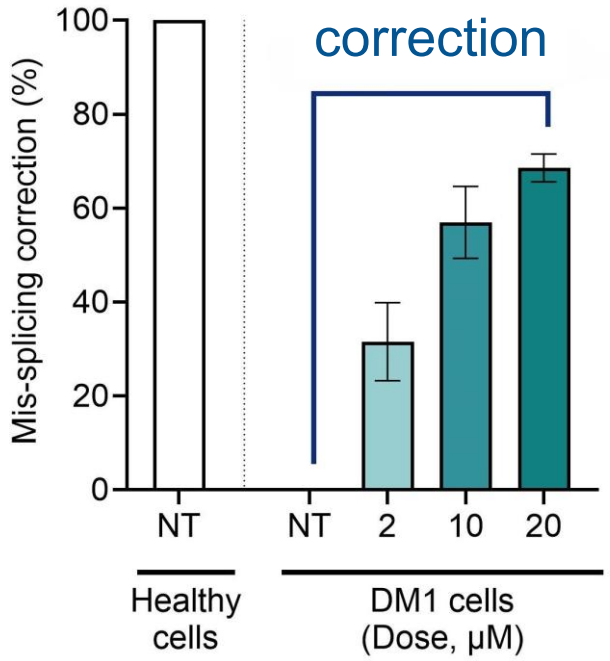
PGN-EDODM1 Treated



Mis-Splicing Correction

Across multiple transcripts

69%
correction



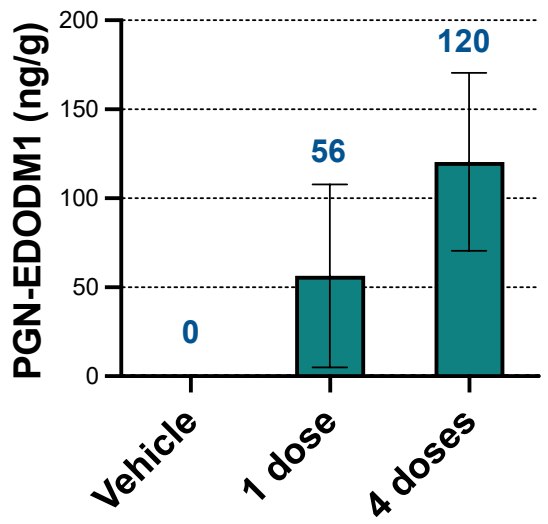
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Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis (QIAxcel) analysis were performed. Visualization with FISH and immunofluorescence microscopy. Mean ± SD; n = 5 per group.

Multiple Doses of PGN-EDODM1 Led to Greater Improvement in Splicing Correction and Myotonia vs Single Dose in Preclinical Studies

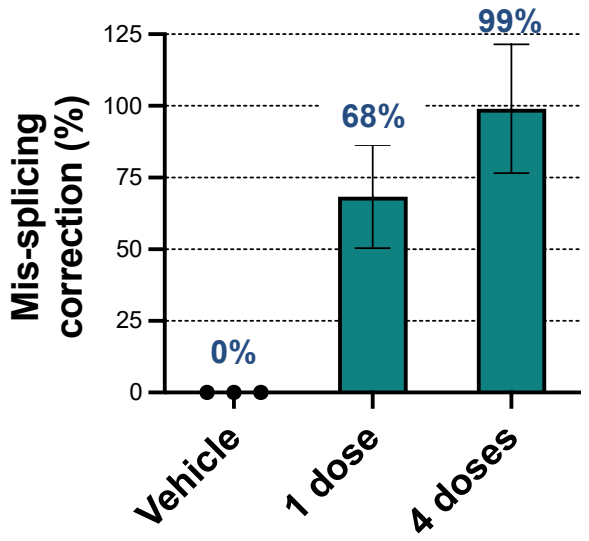
Tissue Concentration

Skeletal muscle



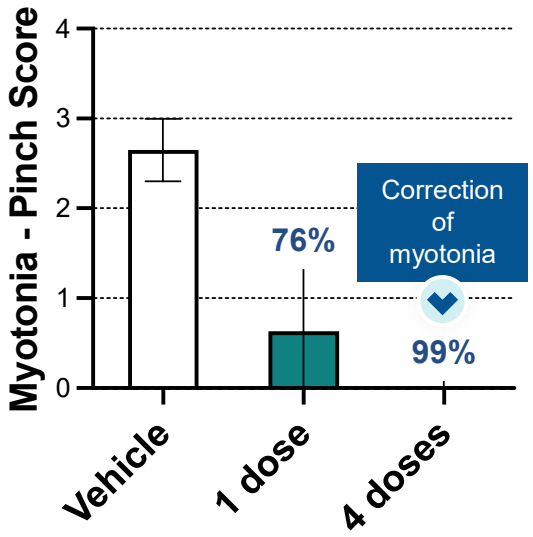
Mis-Splicing Correction

Across multiple transcripts



Correction of Myotonia

Pinch test



Protocol: HSA^{LR} mice received 1 or 4 doses of PGN-EDODM1, with 4-week intervals between doses. Skeletal muscle tissues were collected 4 weeks post-final dose. Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Graph is presented as mean ± SD; n = 8-12 per cohort. Mis-splicing analysis considers multiple transcripts. Graph is presented as mean ± SD; n = 8-12 per cohort per transcript. Action myotonia evaluation (pinch test) was performed 4 weeks post-final dose. Grade 3 = Clear sign of myotonia strong AND reproducible, Grade 2 = Clear sign of myotonia, strong OR reproducible, Grade 1 = Clear sign of myotonia but non reproducible, Grade 0 = No sign of myotonia. Graphs are presented as mean ± SD; n = 12-43 per cohort.

PGN-EDODM1 Clinical Program

FREEDOM2: Phase 2 MAD Study Design

Freedom 2
DM1

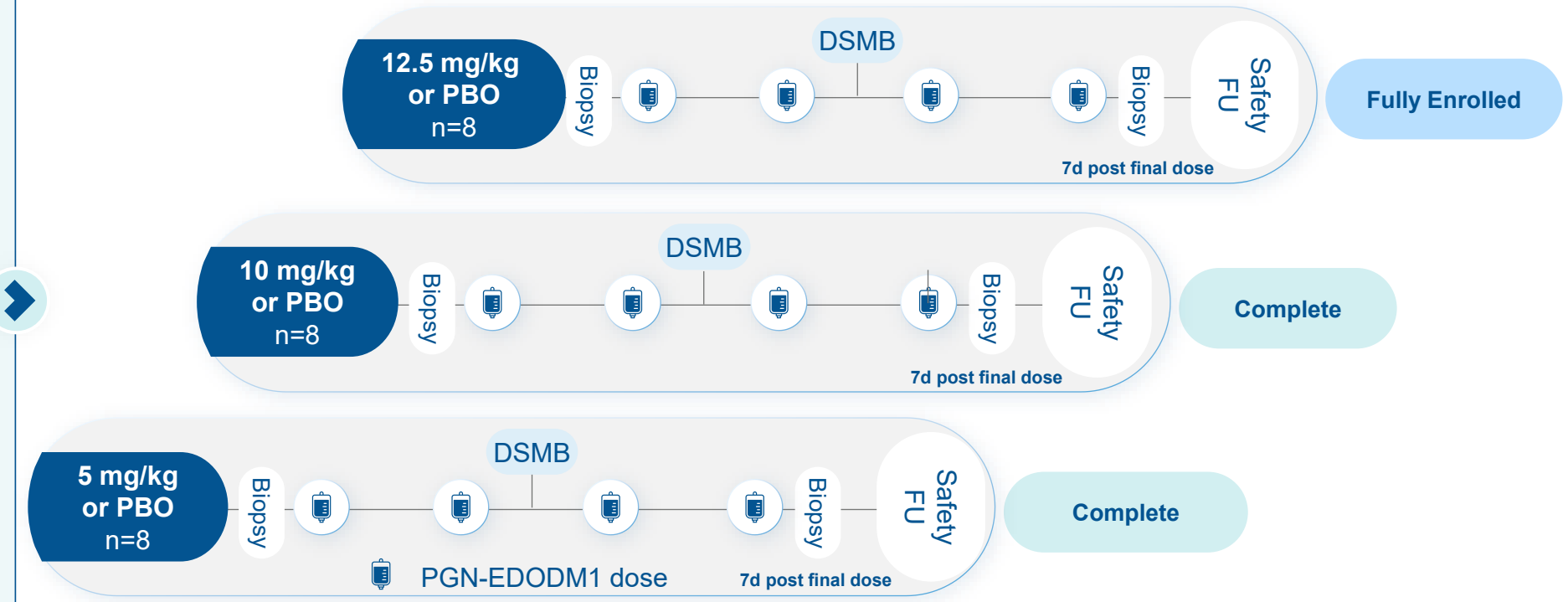
MAD study open in Canada, UK, New Zealand, Australia, and South Korea[1]

IV administration of PGN-EDODM1 or placebo every 4 weeks for a period of 12 weeks

FREEDOM-OLE open for participants from FREEDOM & FREEDOM2

Expansion cohort running in parallel to 12.5 mg/kg cohort will generate longer term data (up to 9 months)

4 Doses of PGN-EDODM1 or Placebo (randomized 3:1)



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[1]The U.S. FDA placed a partial clinical hold on FREEDOM2-DM1 citing nonclinical findings in mice; no U.S. participants dosed in the FREEDOM2-DM1 study to date
DSMB: data safety monitoring board; FU: follow-up; IV: intravenous; MAD: multiple-ascending dose; PBO: placebo; OLE: open label extension

PGN-EDODM1 MAD 10 mg/kg Cohort Reported Best-In-Class Splicing with Improvements Across Myotonia, Mobility, and Grip Strength

1 Highest level of splicing correction reported in a multiple dose study
- 46.5% mean change in splicing at week 13
- 5 of 6 patients improved more than 20% natural variability range[1]; 4 of 6 patients above 50% splicing correction

2 Mechanism linked to function
- vHOT improved 4.3 seconds at Week 13 and 3.9 seconds at Week 16, highest improvement reported at 3 or 6 months
- Associated with splicing correction of CLCN1, a muscle chloride channel driving myotonia in DM1

3 Benefit across proximal and distal muscle groups
- Improvement in mobility and balance as measured by TUG, with the highest improvement reported at 3 or 6 months
- Encouraging improvement in hand grip strength and 10MWRT

4 Clear dose response
- Large improvement in splicing correction and functional endpoints at 10 mg/kg relative to 5 mg/kg

5 Favorable safety
- No SAEs, AESIs, DLTs, or discontinuations; all AEs mild or moderate

[1]PepGen's analysis of natural history data of 114 patients from C Thornton et al., Lancet Neurology 2023; 22: 218–28. Supplement
MAD: Multiple ascending dose; vHOT: video Hand Opening Time; TUG: Timed Up and Go; 10MWRT: 10-Meter Walk/Run Test; SAE: Serious adverse event; AESI: Adverse event of special interest; DLT: Dose limiting toxicity; AE: Adverse event

Consistent, Favorable Safety Profile of PGN-EDODM1 at 5 and 10 mg/kg

Summary of Treatment Emergent Adverse Events (TEAEs)[1]	5 mg/kg (n=8) n (%)	10 mg/kg (n=8) n (%)
Any TEAE	7 (87.5)	8 (100)
Mild	4 (50.0)	4 (50.0)
Moderate	3 (37.5)	4 (50.0)
Severe	0 (0.0)	0 (0.0)
Any SAE	0	0
Any related SAE	0	0
Any AESI or dose-limiting toxicities	0	0
Any TEAE leading to study withdrawal	0	0
Any TEAE leading to death	0	0

PGN-EDODM1 was Generally Well Tolerated, with All AEs Mild or Moderate in Severity[1]

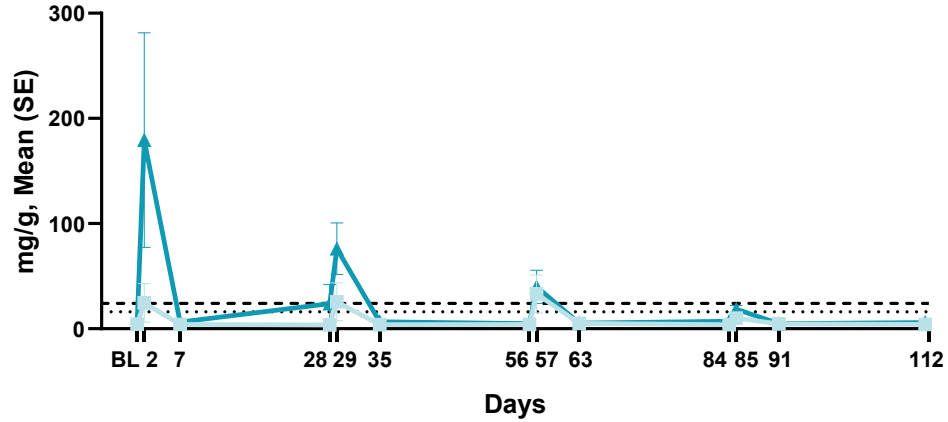
- All participants completed all 4 doses
- Nausea was the most common AE
- No SAEs, AESIs, or DLTs
- Four renal TEAEs reported across two participants, all were mild
- eGFR and creatinine measurements remained stable
- Transient albuminuria improved with subsequent doses
- No notable changes in liver or hematological values and no cardiovascular events
- No anti-drug antibodies detected

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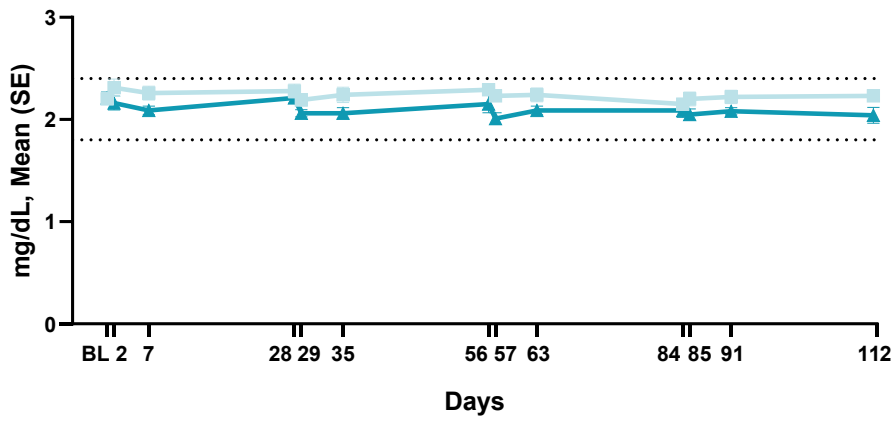
[1]Data cutoff date: 17 Sept 2026
AE: Adverse event; AESI: Adverse event of special interest; DLT: Dose limiting toxicities; SAE: Serious adverse event; TEAE: Treatment emergent adverse event; eGFR: estimated Glomerular Filtration Rate

Renal Biomarker Analysis Supports Favorable Safety Profile

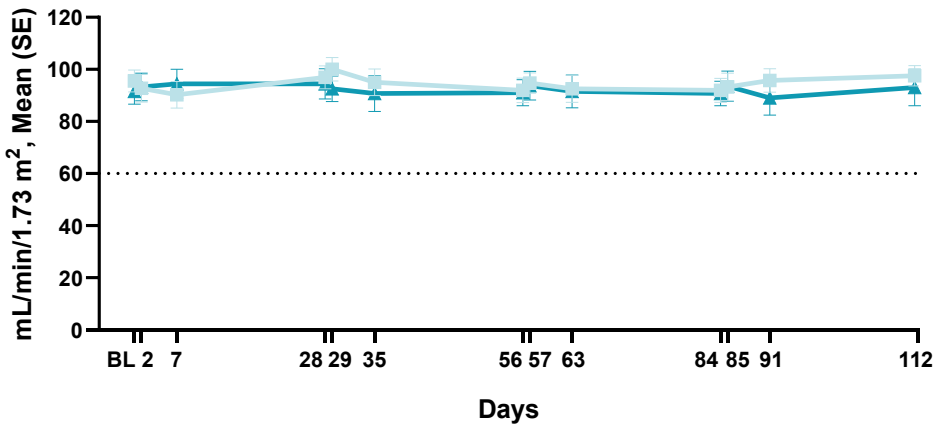
UACR



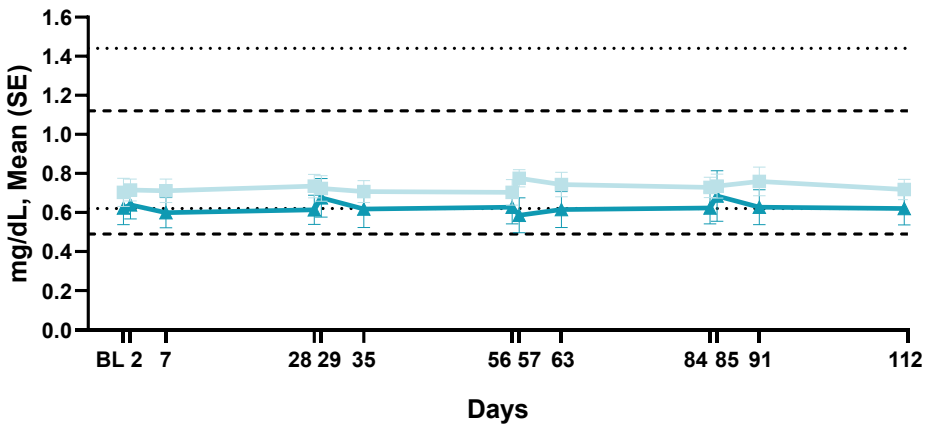
Magnesium[1]



eGFR (Cystatin C)



Serum Creatinine[2]



Cohort 1:
5 mg/kg (n = 6) or Placebo (n = 2), Total n = 8

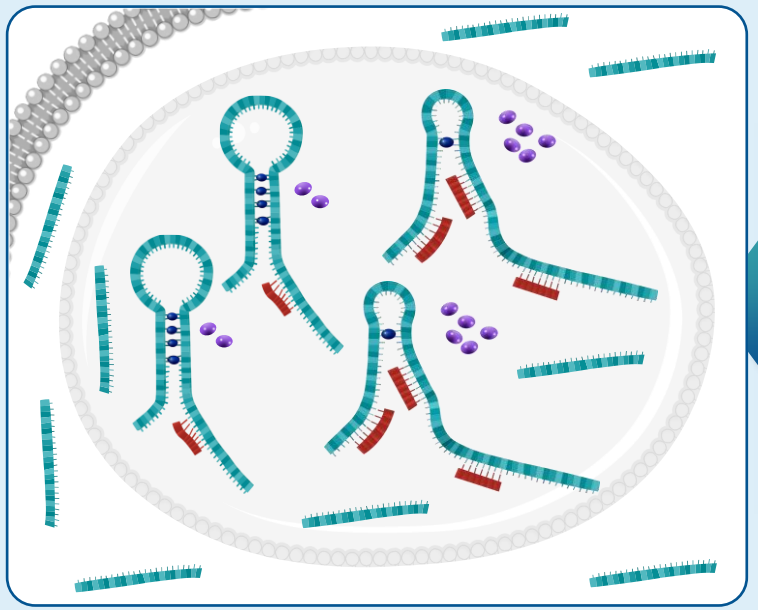
Cohort 2:
10 mg/kg (n = 6) or Placebo (n = 2), Total n = 8

[1]Magnesium: One participant showed a decrease in serum magnesium at a single timepoint at 10mg/kg
[2]Serum Creatinine: One participant at 10mg/kg at a single timepoint went above the upper limit of normal and returned to normal 24 hours later
Horizontal dotted and dashed lines represent the laboratory-defined upper or lower limit of normal for adult males and females, respectively
UACR: Urine albumin-to-creatinine ratio; eGFR: estimated Glomerular Filtration Rate; SE: standard error

PGN-EDODM1 is Designed to Target the Root Cause of DM1

DMPK CTG Expansion → MBNL Sequestration → RNA Mis-splicing → DM1 Disease Manifestations

PGN-EDODM1 binds selectively to the pathogenic *DMPK* transcript, resulting in splicing correction



Liberated MBNL1 restores correct splicing



~11% of Untreated DM1 Patients Demonstrate >20% Splicing Improvement over a 2 to 3 Month Time Period

Natural History Data in Untreated DM1 Patients[1]

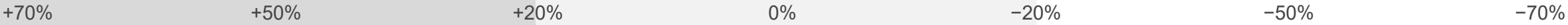
~15%
OF UNTREATED PATIENTS
>20%
Worse

~74%
OF UNTREATED PATIENTS
±20%
Splicing Midrange

~11%
OF UNTREATED PATIENTS
>20%
Correction

Splicing Worsens (% Change from Baseline)

Splicing Improves (% Change from Baseline)



> +70%
OUTLIER
occurs in
<2.6%
of cases
in natural history

Majority
of untreated patients demonstrate
±20% splicing change from baseline
over 2-3 months

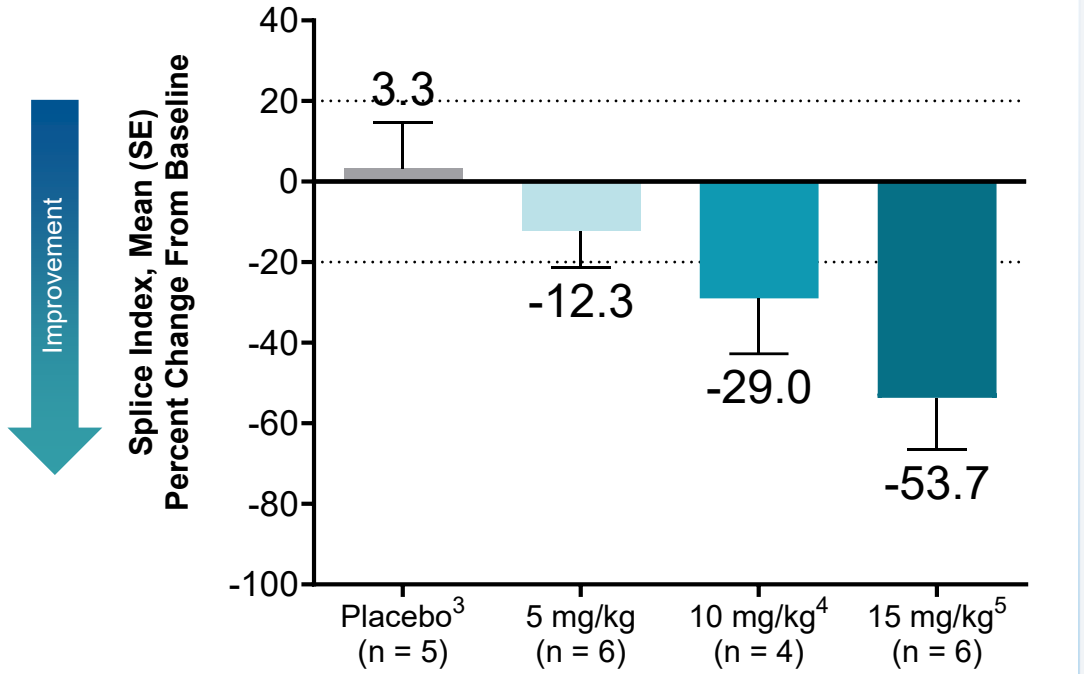
Few
untreated patients demonstrate
>20% splicing change from baseline
over 2-3 months

[1]PepGen's analysis of natural history data of 114 patients from C Thornton et al., Lancet Neurology 2023; 22: 218–28. Supplement

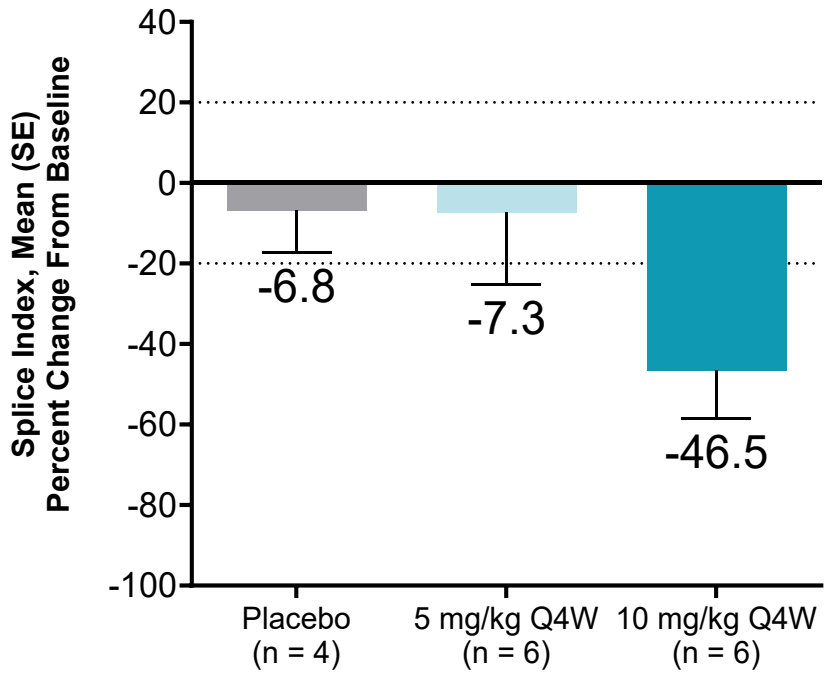
PGN-EDODM1: Highest Splicing Correction Reported in a Multiple Dose Study Demonstrates Robust Target Engagement

FREEDOM SAD
FREEDOM2 MAD

FREEDOM SAD Study[1]



FREEDOM2 MAD Study[2]

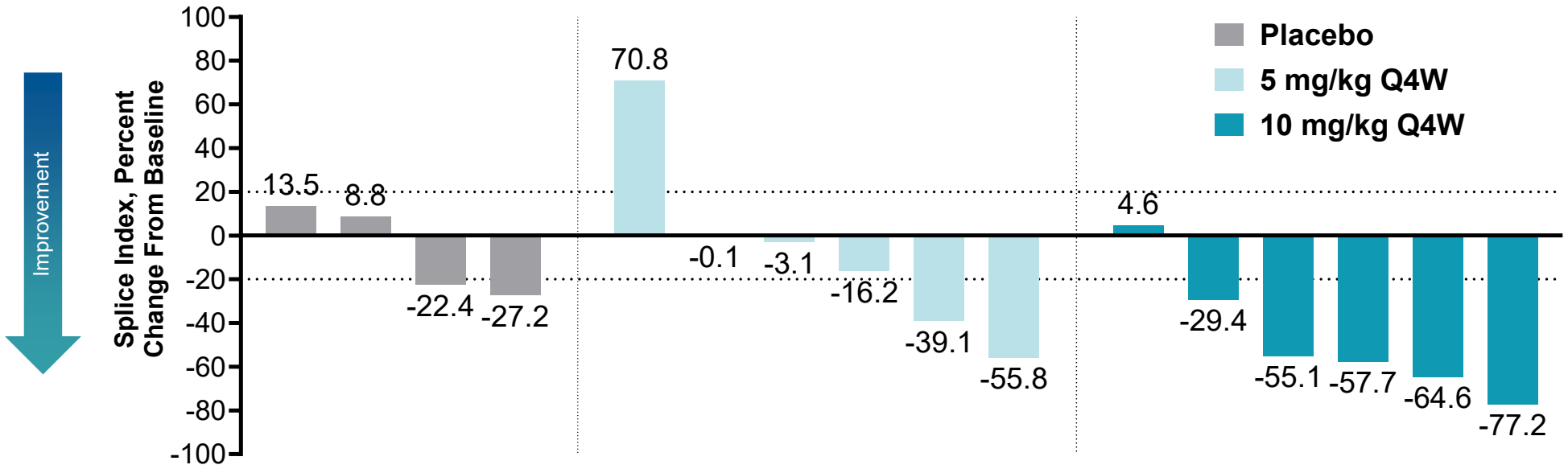


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[1] DM1 Splicing index at day 28 analysis from the single ascending dose (SAD) study
[2] DM1 Splicing index at day 7 following the fourth dose from the multiple ascending dose (MAD) study
[3]Missing sample due to unavailability of biopsy tissue.
[4]One subject at 10 mg/kg biopsy was not collected at day 28 due to pseudoaneurysm in connection with biopsy; one participant's splicing index fell below pre-specified assay range at baseline and day 28 (indicating no detectable mis-splicing)
[5]One subject at 15mg/kg received 77% of the dose, was still included in the splicing index change analysis for the cohort
Q4W: One dose every 4 weeks; SE: standard error

PGN-EDODM1 Splicing Correction Exceeds Natural Splicing Variability[1] in 5 of 6 Participants at 10 mg/kg

Splicing Index Changes: 22-Gene Panel[2]



4 of 6

participants at 10 mg/kg showed improved splicing greater than 50%

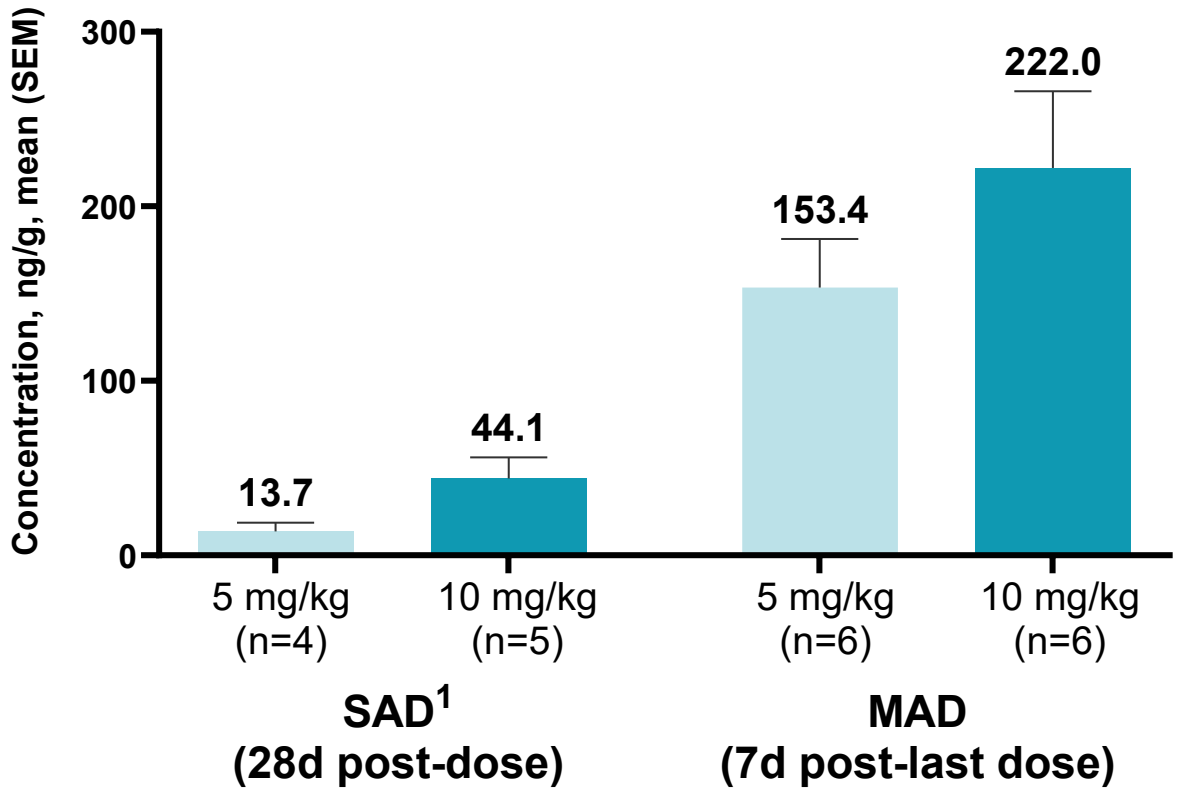
DM1 Splicing index at day 7 following the fourth dose from FREEDOM2-DM1 clinical study; Q4W: One dose every 4 weeks

[1]PepGen's analysis of natural history data of 114 patients from C Thornton et al., Lancet Neurology 2023; 22: 218–28. Supplement; such natural splicing variability represented by +/-20% dotted lines on graph

[2]Provenzano et al., The Splice Index as a prognostic biomarker of strength and function in myotonic dystrophy type 1, J Clin. Invest. 2025

Repeated Dosing of PGN-EDODM1 Increased Muscle Tissue Levels

TA Muscle Tissue Concentration



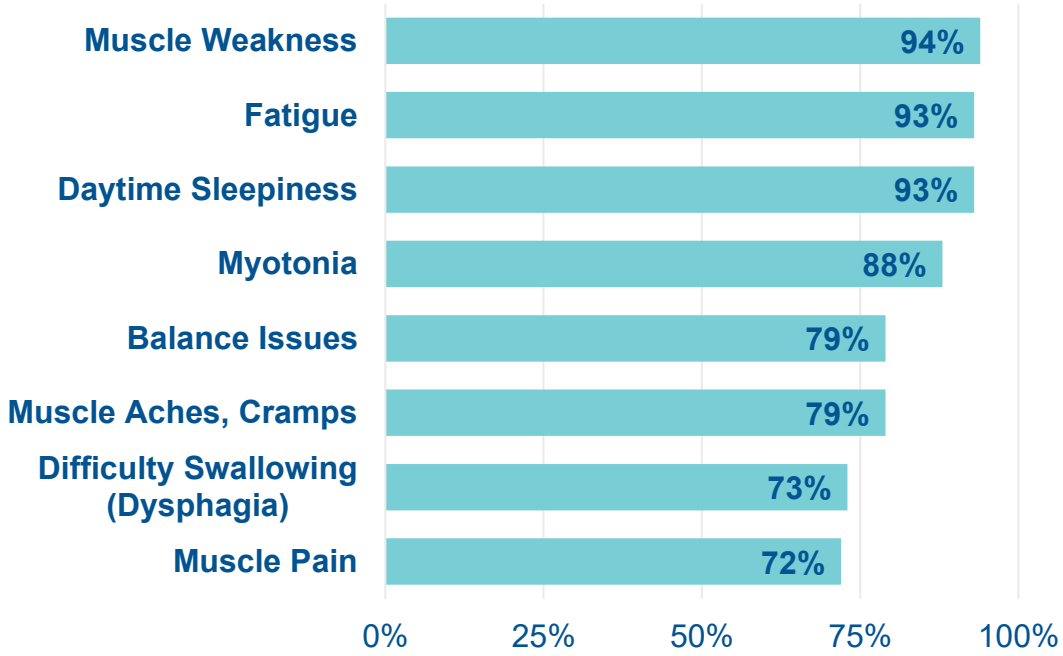
28d or 7d indicates days following the only dose (SAD) or last dose (MAD 4 dose study)
[1]SAD 5mg/kg group reflects n=4 above the lower limit of quantification (LLOQ) and SAD 10 mg/kg group reflects n=5 due to unavailability of biopsy tissue
SEM: standard error of the mean; TA: Tibialis Anterior

In DM1, Muscle Dysfunction Drives Multisystemic Impact for Patients



Tara and Rhys,
Living with DM1

DM1 Most Prevalent Symptoms[1]

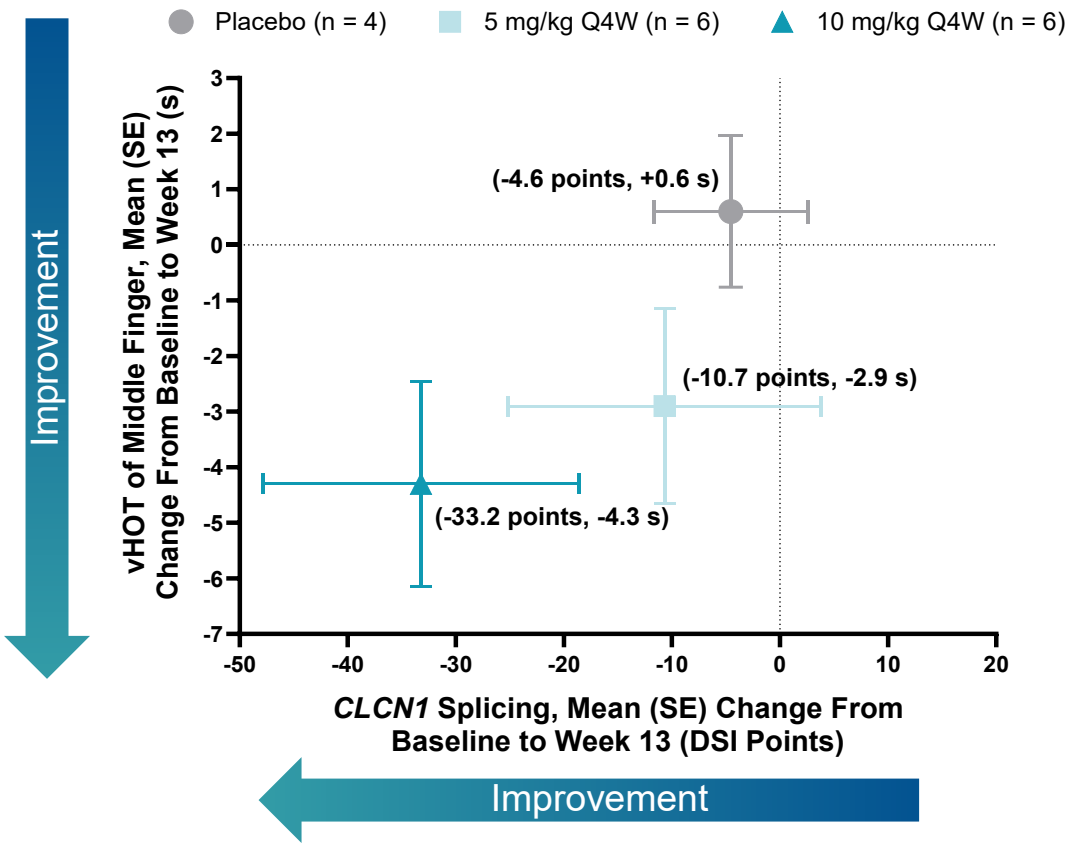


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[1]Christopher Project Reference Group. The myotonic dystrophy experience: a North American cross-sectional study. *Muscle Nerve*. 2019;59(4):457-464. doi:10.1002/mus.26420.

Splicing Correction of CLCN1, a Muscle Chloride Channel, was Associated with Improved Myotonia at 10 mg/kg

vHOT vs *CLCN1* Splicing at 13 Weeks



Mechanism

- *CLCN1* encodes the skeletal muscle chloride channel
- Mis-splicing of *CLCN1* is believed to be a primary driver of myotonia in DM1[1]

Dose-Dependent Improvements

Greater *CLCN1* splicing correction was associated with greater vHOT improvement in a dose-dependent manner

Data illustrate direction only and do not represent a statistical correlation

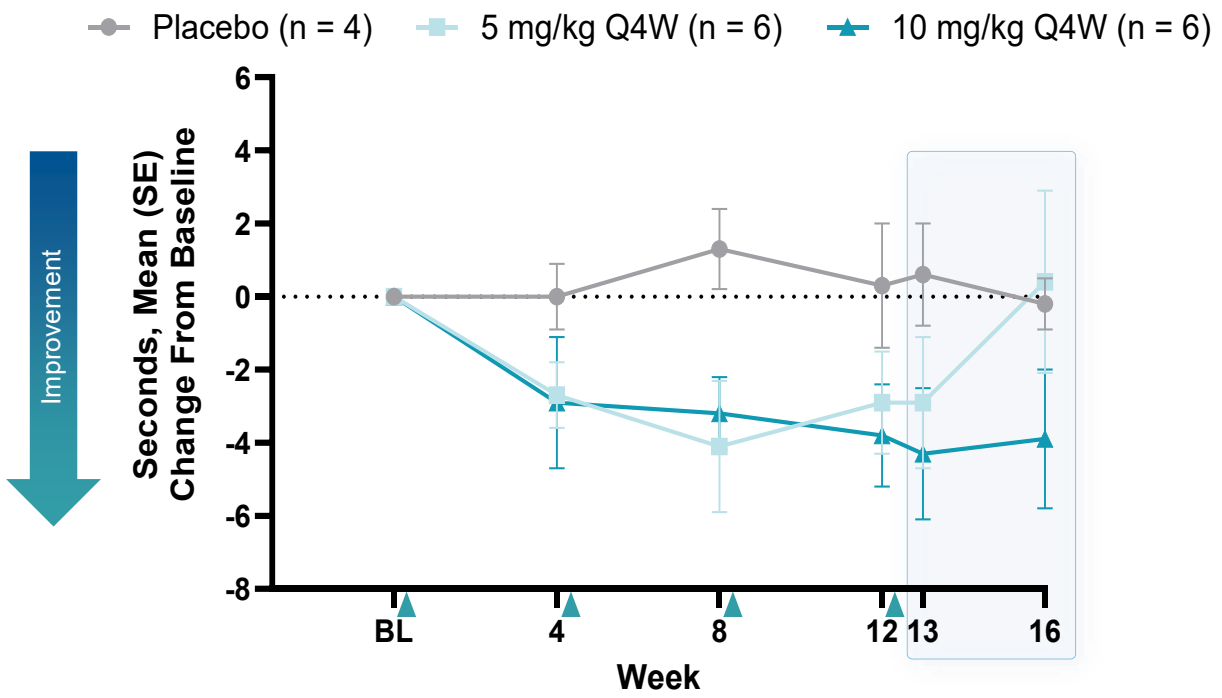
[1]Charlet-B. et al. Mol. Cell, 2002, Vol. 10, 35-44

DSI: DM1 splicing index; Q4W: once every 4 weeks; s: seconds; vHOT: video Hand Opening Time; SE: standard error

Early and Sustained Improvement in Myotonia at 10 mg/kg

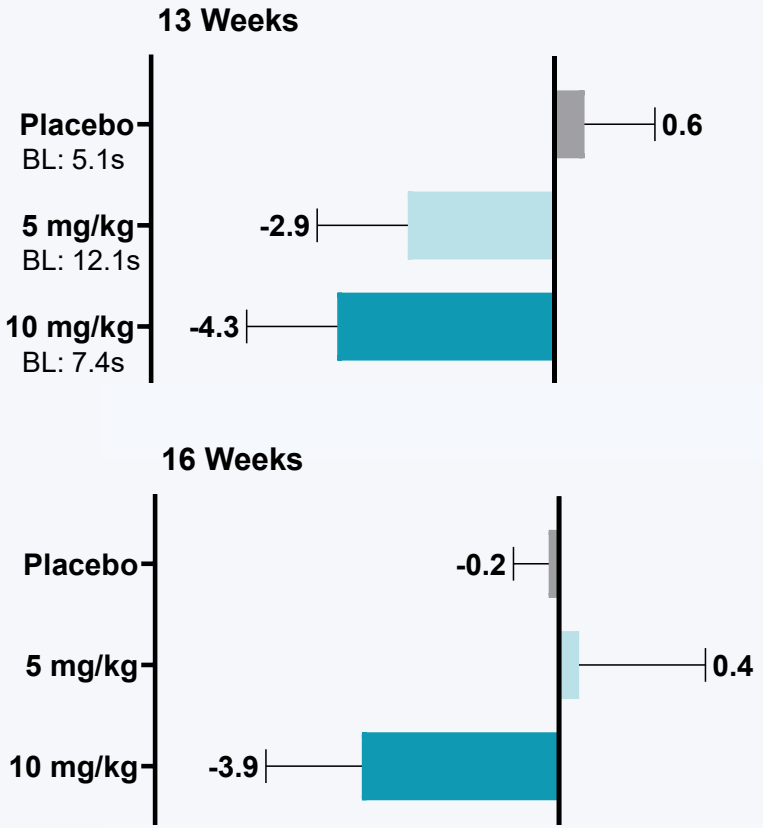
Myotonia measured by video Hand Opening Time (vHOT)

vHOT Analysis



▲ Administration of PGN-EDODM1 (Q4W)

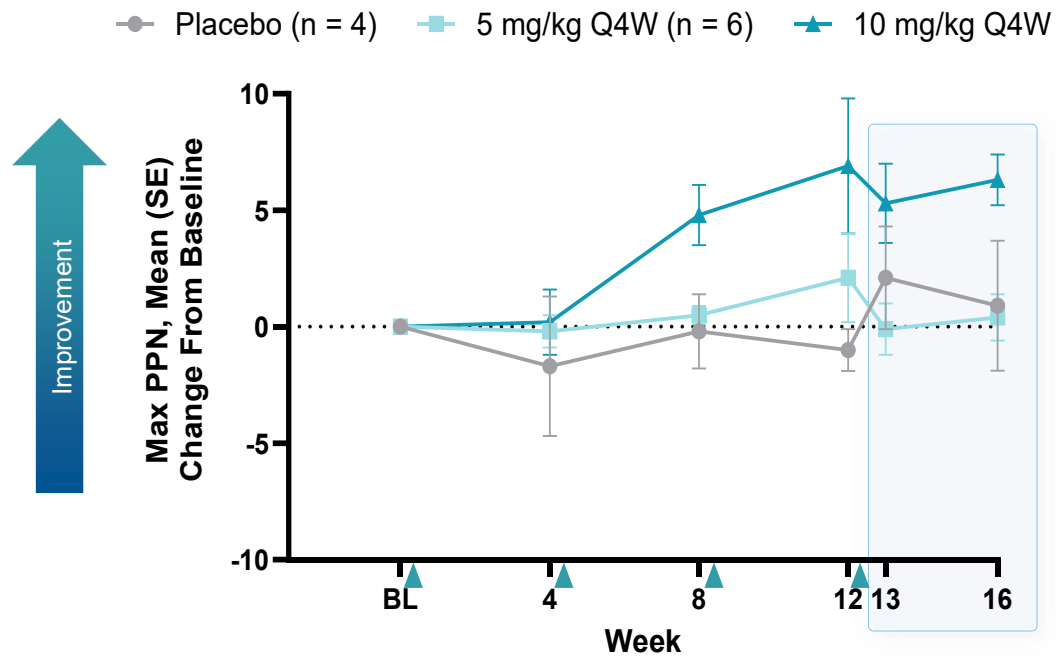
vHOT Change From Baseline (sec)



FREEDOM2 10 mg/kg data plotted two ways: Left panel shows change from baseline over time; Right panel shows change from baseline as a bar graph with mean and standard error of the mean
vHOT analysis is with the middle finger; SE: standard error; Q4W: One dose every 4 weeks; BL: baseline

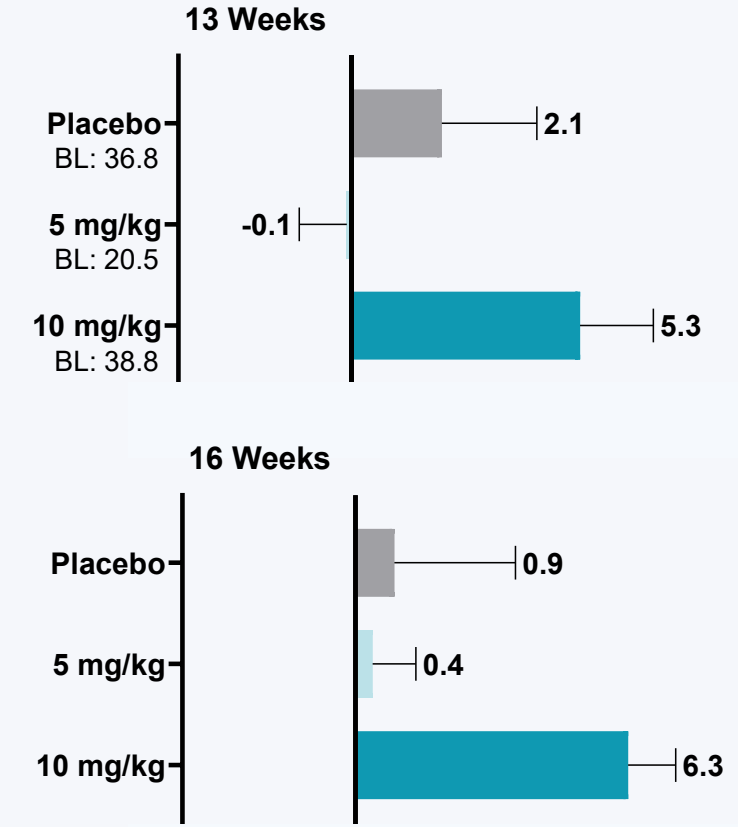
Continued Improvement in Hand Grip Strength Through Week 16

Hand Grip Strength Analysis



▲ Administration of PGN-EDODM1 (Q4W)

Hand Grip Change From Baseline (max PPN)

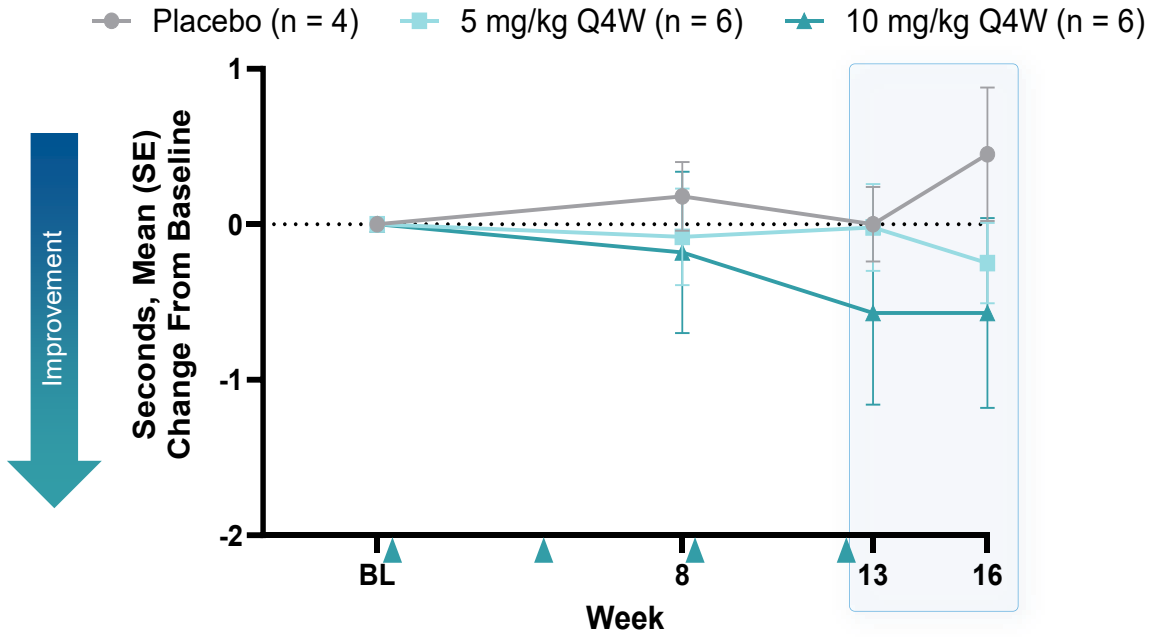


FREEDOM2 10 mg/kg data plotted two ways: Left panel shows change from baseline over time; Right panel shows change from baseline as a bar graph with mean and standard error of the mean
PPN: percent predicted normal; SE: standard error; Q4W: One dose every 4 weeks; BL: baseline

Sustained Improvement in Transitional Balance and Mobility

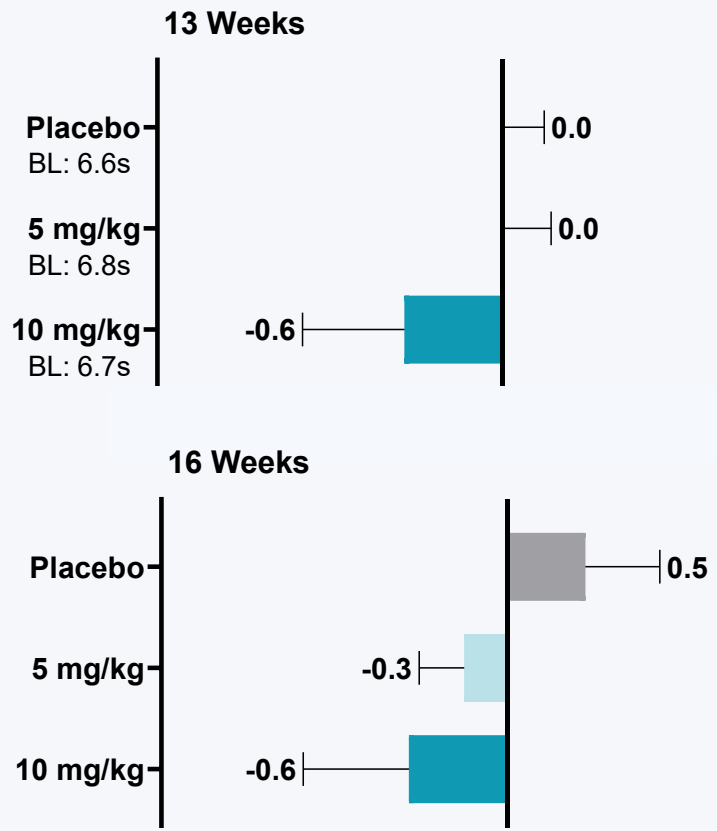
Mobility measured by Timed Up and Go (TUG)

Timed Up and Go Analysis



TUG measures how long it takes someone to stand up from a chair, walk 3 meters, turn around, walk back, and sit down again

TUG Change From Baseline (sec)



▲ Administration of PGN-EDODM1 (Q4W)

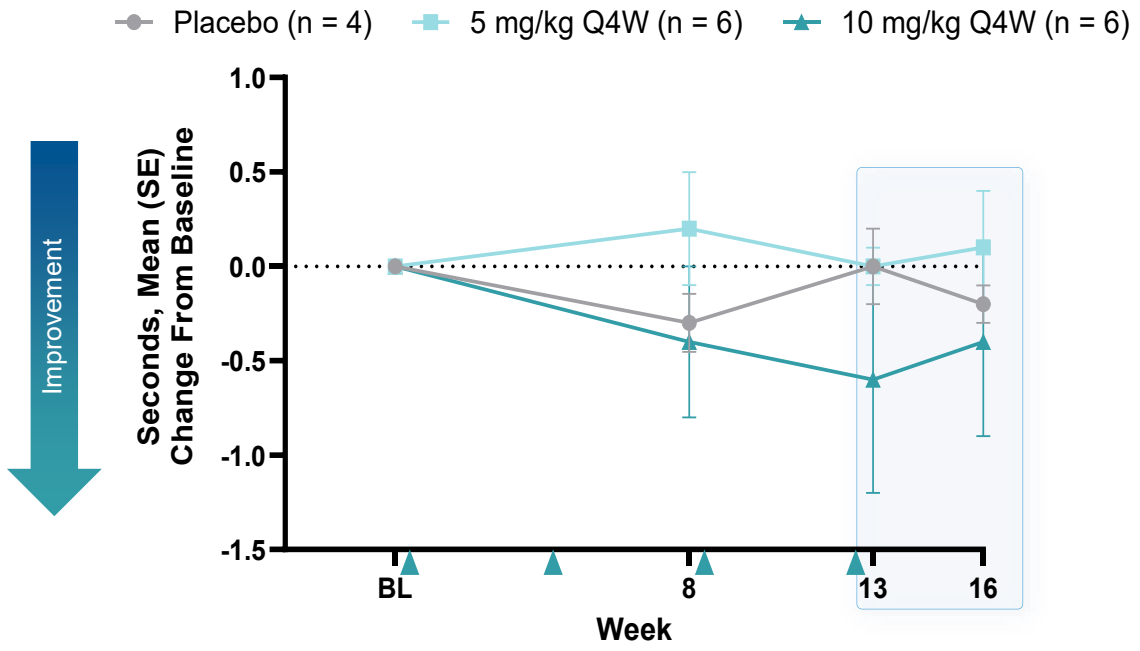
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FREEDOM2 10 mg/kg data plotted two ways: Left panel shows change from baseline over time; Right panel shows change from baseline as a bar graph with mean and SEM
Week 12 was not collected for this endpoint; SE: standard error Q4W: One dose every 4 weeks; BL: baseline

Consistent Gains in 10MWRT at 10 mg/kg at All Timepoints

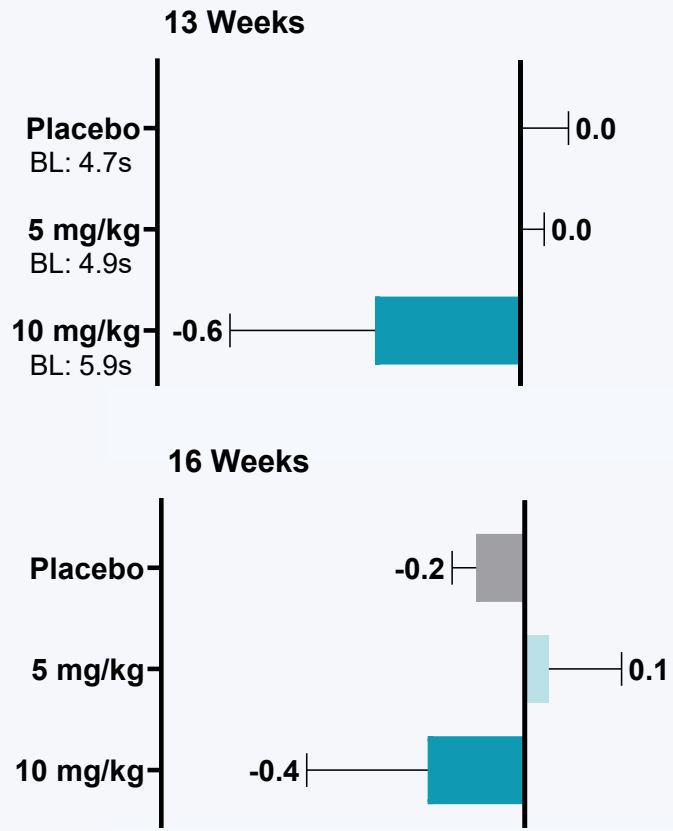
Ambulation measured by 10-Meter Walk/Run Test (10MWRT)

10-Meter Walk/Run Test Analysis



10MWRT measures the time it takes a person to walk or run 10 meters

10MWRT Change From Baseline (sec)



▲ Administration of PGN-EDODM1 (Q4W)

FREEDOM2 10 mg/kg data plotted two ways: Left panel shows change from baseline over time; Right panel shows change from baseline as a bar graph with mean and SEM
Week 12 was not collected for this endpoint; SE: standard error Q4W: One dose every 4 weeks; BL: baseline

Highest Reported Splicing Correction in a Multidose Study and Improvement in Mobility, Myotonia, and Strength, with Favorable Safety Profile Observed at 10 mg/kg

46.5%
Improved Splicing Correction

- 5 of 6 patients improved >20%
- 4 of 6 patients improved >50%
- PBO improved 6.8% at 13 weeks

52.7%
Reduced Myotonia (vHOT)

- **3.9s** improvement at 16 weeks
- **4.3s** improvement at 13 weeks
- PBO improved 0.2s at 16 weeks

16.2%
Improved Hand Grip Strength

- **6.3** max PPN CFB at 16 weeks
- **5.3** max PPN CFB at 13 weeks
- PBO improved 0.9 PPN CFB at 16 wks

8.5%
Improved Timed Up and Go

- **0.6s** improvement at 16 weeks
- **0.6s** improvement at 13 weeks
- PBO worsened 0.5s at 16 weeks

6.8%
Improved 10m Walk/Run Test

- **0.4s** improvement at 16 weeks
- **0.6s** improvement at 13 weeks
- PBO improved 0.2s at 16 weeks

0
Serious, severe, or dose limiting TEAEs

- No discontinuations
- No SAEs

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10 mg/kg n=6, placebo pooled n=4; Percent improvement values are shown as week 13 for splicing, and week 16 for all other endpoints. Percentage improvement was calculated by dividing mean change at 16-week by mean baseline for all functional endpoints. PBO, Placebo; vHOT, video Hand Opening Time; wks, weeks; PPN, percent predicted normal; CFB, Change from Baseline

FREEDOM2 Phase 2 Execution Creates a Sequence of Clinical and Regulatory Value Inflections in 2027 And Beyond

PEPGEN'S AMBITION:

Reach broadly.

Reset disease-driving RNA.

Pursue meaningful restoration for patients.

FREEDOM2 MAD AND FREEDOM-OLE

FREEDOM2 Cohort 3 (12.5 mg/kg): Fully enrolled, participants have received up to 3 doses

Open-label Extension (OLE): >35 doses at 10 mg/kg and >100 doses at 5 mg/kg have been delivered

- 20 total participants enrolled to date*
- No SAEs, no DLTs, one discontinuation due to hypersensitivity reaction

Building upon the positive results seen at 10 mg/kg, PepGen plans to initiate an expansion cohort, running in parallel to Cohort 3, to generate longer term (up to 9 months) data and evaluate PGN-EDODM1 in additional participants

GUIDANCE:

- **January:** Interim FREEDOM-OLE 5 mg/kg clinical and 10 mg/kg safety data expected
- **1H 2027:** FREEDOM2 12.5 mg/kg clinical results
- **H2 2027**: EOP2 meeting with regulators anticipated pending results of the 12.5 mg/kg cohort to discuss the registrational program, pending partial clinical hold removal

Cash runway into 2029

DLT: Dose limiting toxicities; SAE: Serious adverse event
*As of Nov 19, 2026












Thank You

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